

Amendments to the Claims

This listing of claims is intended to replace all prior versions and listings of claims in the above-identified application.

1. (original) A compound comprising a gonadotrophin releasing hormone (GnRH) analogue conjugated to a hormone moiety, or a derivative thereof, which is able to bind to a plasma hormone binding protein.
2. (original) A compound according to Claim 1 wherein the GnRH analogue is a peptide analogue.
3. (original) A compound according to Claim 2 wherein the GnRH analogue is a nonapeptide or a decapeptide.
4. (currently amended) A compound according to Claim 1 ~~any of the preceding claims~~ wherein one of the amino acid residues of the GnRH analogue is a D-amino acid.
5. (currently amended) A compound according to Claim 4 ~~any of the preceding claims~~ wherein the D-amino acid is D-Lys.
6. (currently amended) A compound according to Claim 4 ~~any of Claims 4 or 5~~ wherein the D-amino acid is at position 6.
7. (currently amended) A compound according to Claim 1 ~~any of Claims 1 to 6~~ wherein the GnRH analogue is a GnRH antagonist.
8. (original) A compound according to Claim 7 wherein the GnRH antagonist is [AcD-Nal¹, D-Cpa², D-Pal³, Arg⁵, D-Lys⁶, D-Ala¹⁰]GnRH, or [Ac-ΔPro¹, D-Fpa², D-Trp³, D-Lys⁶]GnRH.
9. (original) A compound according to Claim 7 wherein the GnRH antagonist is Cetrorelix, Ganirelix, Abarelix, Antide, Teverelix, FE200486, Na-Glu, A-75998, A-76154, A-84861, D-26344, D-63153, D21775, ramorelix, degarelix, NBI-42902, Org-30850, detirelix, iturelix, TAK-013, TAK810, AN 207, AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Leu-Arg-Pro-D-Ala-NH₂; Ac-ΔPro-D-Fpa-D-Trp-Ser-Tyr-D-Lys-Leu-Arg-Pro-Gly-NH₂; AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Lys-Leu-Arg-D-Ala-NH₂; D-Pal-Ser-Arg-D-Lys-Leu-Arg-

Pro-D-Ala-NH₂; AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Lys-Arg-Pro-D-Ala-NH₂; [D-Pyr¹, D-Phe², D-Trp³⁻⁶]GnRH; D-Lys⁶Antide; Lys⁵ Antide or Lys⁸ Antide.

10. (currently amended) A compound according to Claim 1 ~~any of Claims 1-6~~ wherein the GnRH analogue is a GnRH agonist.

11. (original) A compound according to Claim 10 wherein the GnRH agonist is pGlu-His-Trp-Ser-Tyr-D-lys-Leu-Arg-Pro-GlyNH₂, Lupron, Zoladex, Supprelin, Synarel, Triptorelin, Buserelin, leuprolide, goserelin, deslorelin, ProMaxx-100, avorelin, histrelin, nafarelin, leuprorelin or triptorelin.

12. (currently amended) A compound according to Claim 1 ~~any of the preceding claims~~ wherein the hormone moiety is a steroid hormone moiety.

13. (original) A compound according to Claim 12 wherein the steroid hormone moiety is estradiol, progesterone, cortisol, corticosterone, estrone, testosterone or dihydroxytestosterone.

14. (original) A compound according to Claim 13 wherein the progesterone derivative is 11 α -hydroxyprogesterone or 21-hydroxyprogesterone.

15. (currently amended) A compound according to Claim 1 ~~any of the preceding claims~~ wherein the compound retains the *in vivo* hormonal activity of the hormone moiety or derivative thereof.

16. (currently amended) A compound according to Claim 1 ~~any of Claims 1-14~~ wherein the compound has no *in vivo* hormonal activity of the hormone moiety or derivative thereof.

17. (currently amended) A compound according to Claim 1 ~~any of the preceding claims~~ wherein the hormone moiety binds to a plasma hormone binding protein *in vivo*.

18. (currently amended) A compound according to Claim 1 ~~any of the preceding claims~~ wherein the hormone binding protein is a globulin.

19. (original) A compound according to Claim 18 wherein the plasma hormone binding protein is cortisol binding globulin (CBG), sex hormone binding globulin (SHBG), or progesterone binding globulin (PBG) or albumin.

20. (currently amended) A compound according to Claim 1 ~~any of Claims 1-19~~ wherein the conjugated GnRH analogue and the hormone moiety are cleavable.

21. (currently amended) A compound according to Claim 1 ~~any of Claims 1-19~~ wherein the GnRH analogue and the hormone moiety are directly conjugated.

22. (currently amended) A compound according to Claim 1 ~~any of Claims 1-20~~ wherein the GnRH analogue and the hormone moiety are conjugated via a linking group.

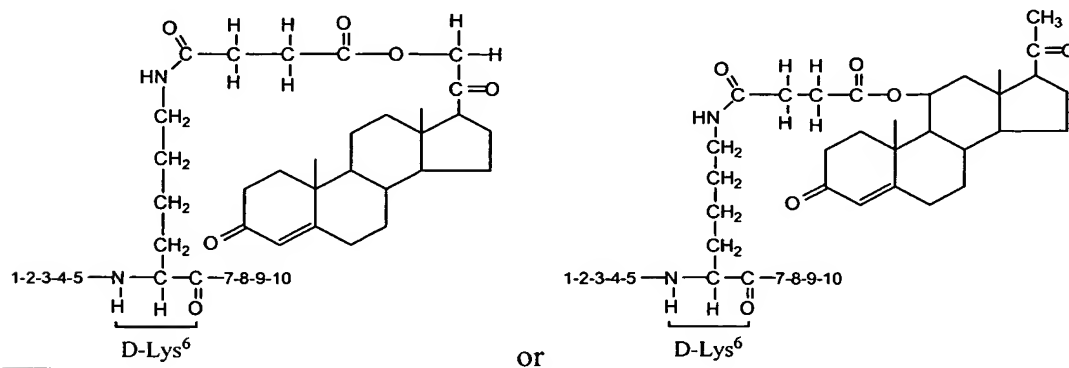
23. (currently amended) A compound according to Claim 22 wherein the linking group comprises linker ~~linker~~ is a succinate linker or a derivative thereof.

24. (currently amended) A compound according to Claim 1 ~~any of the preceding claims~~ wherein the GnRH analogue has a D-lysine residue, and the GnRH analogue is conjugated to the hormone moiety via the D-lysine.

25. (currently amended) A compound according to Claim 1 ~~any of the preceding claims~~ which has a longer half-life *in vivo* than native GnRH.

26. (currently amended) A compound according to Claim 1 ~~any of the preceding claims~~ which has a longer duration of activity *in vivo* than native GnRH.

27. (currently amended) A compound according to Claim 1 having the formula shown in Figure 1A or 1B



28. (currently amended) A compound according to Claim 1 which is: AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Leu-Arg-Pro-D-Ala-NH₂ conjugated to 21-hydroxyprogesterone 21-succinate at the ϵ amine of D-Lys at position 6; Ac- Δ Pro-D-Fpa-D-Trp-Ser-Tyr-D-Lys-Leu-Arg-Pro-Gly-NH₂ conjugated to 21-hydroxyprogesterone 21-succinate at the ϵ amine of D-Lys at position 6; AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Lys-Leu-Arg-D-Ala-NH₂ conjugated to 21-hydroxyprogesterone 21-succinate at the ϵ amine of Lys at position 7; D-Pal-Ser-Arg-D-Lys-Leu-Arg-Pro-D-Ala-NH₂ conjugated to 21-hydroxyprogesterone 21-succinate at the N-terminal amine of D-Pal; AcD-Nal-D-Cpa-D-Pal-Ser-Arg-D-Lys-Lys-Arg-Pro-D-Ala-NH₂ conjugated to 21-hydroxyprogesterone 21-succinate at the ϵ amine of Lys at position 7; or [DLys⁶]GnRH conjugated to 11 α -hydroxyprogesterone 11-succinate at the ϵ amine group of the D-Lys at position 6.

29. (currently amended) A compound according to Claim 1 ~~any of the preceding claims~~ which is bound to a plasma hormone binding protein.

30. (original) A compound according to Claim 29 wherein the plasma hormone binding protein is CBG, SHBG, or albumin.

31. (currently amended) A pharmaceutical composition comprising a compound according to Claim 1 ~~any of Claims 1-30~~ and a pharmaceutically acceptable excipient, carrier or diluent.

32. (original) A pharmaceutical composition according to Claim 31 which is suitable for oral administration.

33. (original) A pharmaceutical composition according to Claim 31 which is a slow-release formulation.

34. (canceled)

35. (currently amended) A method of reducing the fertility of an individual comprising administering a compound according to Claim 1 ~~any of Claims 1-30, or a pharmaceutical composition according to any of Claims 31-33,~~ to the individual.

36. (canceled)

37. (currently amended) A method of combating a hormone-dependent disease or condition comprising administering a compound according to Claim 1 ~~any of~~

~~Claims 1-30, or a pharmaceutical composition according to any of Claims 31-33, to an individual in need thereof.~~

38. (canceled)

39. (currently amended) A method according to Claim 37 ~~or a use according to Claim 38~~ wherein the hormone-dependent disease or condition is selected from a hormone-dependent cancer, benign prostatic hypertrophy, endometriosis, uterine fibroids, premenstrual syndrome, polycystic ovarian syndrome, hirsutism, acne vulgaris, precocious puberty, acute intermittent porphyria, cryptorchidism and delayed puberty.

40. (currently amended) A method ~~or a use~~ according to Claim 39 wherein the hormone-dependent cancer is breast cancer, prostate cancer, uterine cancer or endometrial cancer.

41. (currently amended) A method of combating infertility comprising administering a compound according to Claim 1 ~~any of Claims 1-30, or a pharmaceutical composition according to any of Claims 31-33,~~ to an individual in need thereof.

42. (canceled)

43. (currently amended) A method of modulating the production of gonadotrophins or sex hormones *in vivo* comprising administering a compound according to Claim 1 ~~any of Claims 1-30, or a pharmaceutical composition according to any of Claims 31-33,~~ to an individual.

44. (canceled)

45. (original) A method of modifying a GnRH analogue so that it has an increased *in vivo* half-life compared to GnRH, the method comprising conjugating the GnRH analogue to a hormone moiety, or a derivative thereof, which is able to bind to a plasma hormone binding protein.

46. (original) A method of modifying a GnRH analogue so that it has an increased duration of activity *in vivo* compared to GnRH, the method comprising conjugating the GnRH analogue to a hormone moiety, or a derivative thereof, which is able to bind to a plasma hormone binding protein.

47. (currently amended) A method according to Claim 45 ~~or 46~~ wherein the conjugating step comprises conjugating the GnRH analogue and the hormone moiety or derivative thereof via a linking group.

48. (currently amended) A method according to Claim 45 ~~,46 or 47~~ further comprising binding the hormone moiety or derivative thereof to a plasma hormone binding protein.

49. (original) A method according to Claim 48 wherein the plasma hormone binding protein is CBG, SHBG, or albumin.

50. (currently amended) A method according to Claim 45 ~~any of Claims 46-59~~ further comprising determining the *in vivo* half-life ~~or duration of activity~~ of the conjugated GnRH analogue.

51. (currently amended) A method according to Claim 50 further comprising comparing the *in vivo* half-life ~~or duration of activity~~ of the conjugated GnRH analogue with the *in vivo* half-life ~~or duration of activity~~ of GnRH to identify a GnRH analogue having an increased *in vivo* half-life ~~or duration of activity~~ compared to GnRH.

52. (new) A method according to Claim 35 wherein the compound is present in a pharmaceutical composition that comprises a pharmaceutically acceptable excipient, carrier or diluent.

53. (new) A method according to Claim 37 wherein the compound is present in a pharmaceutical composition that comprises a pharmaceutically acceptable excipient, carrier or diluent.

54. (new) A method according to Claim 41 wherein the compound is present in a pharmaceutical composition that comprises a pharmaceutically acceptable excipient, carrier or diluent.

55. (new) A method according to Claim 43 wherein the compound is present in a pharmaceutical composition that comprises a pharmaceutically acceptable excipient, carrier or diluent.

56. (new) A method according to Claim 46 wherein the conjugating step comprises conjugating the GnRH analogue and the hormone moiety or derivative thereof via a linking group.

57. (new) A method according to Claim 56 further comprising binding the hormone moiety or derivative thereof to a plasma hormone binding protein.

58. (new) A method according to Claim 57 wherein the plasma hormone binding protein is CBG, SHBG, or albumin.

59. (new) A method according to Claim 46 further comprising determining the *in vivo* duration of activity of the conjugated GnRH analogue.

60. (new) A method according to Claim 59 further comprising comparing the *in vivo* duration of activity of the conjugated GnRH analogue with the *in vivo* duration of activity of GnRH to identify a GnRH analogue having an increased *in vivo* duration of activity compared to GnRH.